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1: Proc Natl Acad Sci U S A. 1999 Sep 28;96(20):11364-9. Related Articles, Links

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RING fingers mediate ubiquitin-conjugating enzyme (E2)-dependent ubiquitination.

Lorick KL, Jensen JP, Fang S, Ong AM, Hatakeyama S, Weissman AM.

Laboratory of Immune Cell Biology, Division of Basic Sciences, National Cancer Institute, Building 10, Room 1B34, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20892-1152, USA.

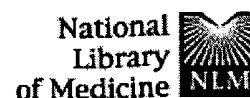
A RING finger-containing protein (AO7) that binds ubiquitin-conjugating enzymes (E2s) and is a substrate for E2-dependent ubiquitination was identified. Mutations of cation-coordinating residues within AO7's RING finger abolished ubiquitination, as did chelation of zinc. Several otherwise-unrelated RING finger proteins, including BRCA1, Siah-1, TRC8, NF-X1, kf-1, and Praja1, were assessed for their ability to facilitate E2-dependent ubiquitination. In all cases, ubiquitination was observed. The RING fingers were implicated directly in this activity through mutations of metal-coordinating residues or chelation of zinc. These findings suggest that a large number of RING finger-containing proteins, with otherwise diverse structures and functions, may play previously unappreciated roles in modulating protein levels via ubiquitination.

PMID: 10500182 [PubMed - indexed for MEDLINE]

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1: Mol Biol Cell. 2000 Jul;11(7):2315-25.

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The APC11 RING-H2 finger mediates E2-dependent ubiquitination.

Levenson JD, Joazeiro CA, Page AM, Huang H, Hieter P, Hunter T.

Molecular Biology and Virology Laboratory, The Salk Institute, 10010 North Torrey Pines Road, La Jolla, California 92037, USA.

Polyubiquitination marks proteins for degradation by the 26S proteasome and is carried out by a cascade of enzymes that includes ubiquitin-activating enzymes (E1s), ubiquitin-conjugating enzymes (E2s), and ubiquitin ligases (E3s). The anaphase-promoting complex or cyclosome (APC/C) comprises a multisubunit ubiquitin ligase that mediates mitotic progression. Here, we provide evidence that the *Saccharomyces cerevisiae* RING-H2 finger protein Apc11 defines the minimal ubiquitin ligase activity of the APC. We found that the integrity of the Apc11p RING-H2 finger was essential for budding yeast cell viability. Using purified, recombinant proteins we showed that Apc11p interacted directly with the Ubc4 ubiquitin conjugating enzyme (E2). Furthermore, purified Apc11p was capable of mediating E1- and E2-dependent ubiquitination of protein substrates, including Clb2p, in vitro. The ability of Apc11p to act as an E3 was dependent on the integrity of the RING-H2 finger, but did not require the presence of the cullin-like APC subunit Apc2p. We suggest that Apc11p is responsible for recruiting E2s to the APC and for mediating the subsequent transfer of ubiquitin to APC substrates in vivo.

PMID: 10888670 [PubMed - indexed for MEDLINE]

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